REMARKS

Currently, claims 28, 30-31, 33-35, 37-38, 40, 42-44, 46, and 62-67 including independent claim 28, are pending in the present application. Independent claim 28, for instance, is directed to a method of utilizing a triggerably releasable delivery system. The method comprises administering to a mucosal membrane of a patient a plurality of nanoparticles containing silica coated with alumina and having a size of about 500 nanometers or less. The alumina provides a site on a surface of the nanoparticles to which is bonded a functional compound. The nanoparticles also possess a positive surface charge, i.e., a zeta potential of about 20 millivolts or more. The nanoparticles are contained within a vehicle that further comprises a pH altering material (e.g., acid or base). The functional compound is released from the surface of the nanoparticles upon exposure to a change in pH.

In the Office Action, the previous claims were initially rejected under *35 U.S.C. § 112*, first paragraph, for failure to comply with the written description requirement with respect to the terms "the treatment of a patient", a "functional compound", and "environmental or chemical condition." Without commenting on the propriety of the rejections relating to the terms "the treatment of a patient" and "environmental or chemical condition", Applicants note that these rejections are moot in that these terms are no longer included in the present claims. Furthermore, Applicants respectfully submit that the term "functional compound" is fully described in the present specification. To satisfy the written description requirement, it is well established that every possible species of a compound need not be disclosed. Instead, the issue is whether the specification describes the claimed invention in sufficient detail that one

skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. In this particular case, the application discloses numerous representative species of the claimed "functional compound", such as tetracycline, baicaline hydrate, baicalein, daunorubicin, salicylanilide, salacetamide, salsalate, albofungin, etc. Based on this description and the examples given, one of ordinary skill in the art would recognize that the Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For at least this reason, it is submitted that the present claims fully satisfy the written description requirement.

The Office Action also rejected the previous claims under *35 U.S.C. § 112*, first paragraph, for failure to enable "all functional compounds." To support a finding that a "functional compound" is not enabled by the present specification, it is the Examiner's burden to show that the specification would not have guided one skilled in the art how to make and/or use functional compounds without undue experimentation. The amount of guidance needed is inversely related to the amount of knowledge in the art. *See M.P.E.P § 2164.03*. In this particular case, numerous functional compounds are disclosed in the present specification. Further, the art is replete with numerous references and teachings of functional compounds (e.g., therapeutic agents) for administering to a mucosal membrane (e.g., vagina) of a patient. One of ordinary skill in the art would certainly expect that the claimed genus of "functional compounds" could be made without undue experimentation. (*M.P.E.P. § 2164.02(b)*). For at least the reasons noted above, Applicants respectfully submit that the present claims satisfy the requirements of *35 U.S.C. § 112*, first paragraph.

Furthermore, in the Office Action, previous dependent claim 43 (now incorporated into independent claim 28) was rejected under *35 U.S.C. § 103(a)* as being obvious over U.S. Patent No. 6,007,795 to Masterman, et al. in view of Ma, et al. (an article entitled Fundamentals of Adsorption." Masterman, et al. is directed to a method for inhibiting bacteria in the mouth of a patient. The method includes placing a particle containing a degradable material (e.g., poly(DL-lactide)-co-glycolide) and an anti-microbial agent into the mouth of a patient. The anti-microbial agent may be dispersed throughout the particle along with the degradable material, enclosed within a skin composed of the material, or attached to a skin composed of the degradable material. (Col. 4, ll. 64-67). Suffice to say, the anti-microbial agent is specifically associated with the degradable material so that it is released only upon its degradation. The particle may also be coated with a water-stable material (e.g., polystyrene) that does not degrade when exposed to saliva. The coating is instead disrupted by brushing, flossing, or chewing, which then exposed the degradable material to saliva and causes the anti-microbial to be released.

Masterman, et al. cursorily mentions that the degradable material can also be included in an organic/inorganic composite that includes a degradable polymer mixed or covalently bound to a mineral. It is on this basis that the Office Action asserts that Masterman, et al. discloses the limitations of independent claim 28. Even if the organic/inorganic composite of Masterman, et al. were somehow akin to the claimed nanoparticles, however, Applicants respectfully point out that independent claim 28 expressly requires that the alumina provides a site on the "surface" of the nanoparticles to which is bonded the functional compound. This is not the case with Masterman, et al.

In fact, if the anti-microbial agent of Masterman, et al. were bonded to a surface of the particle as in the present claims, it would be immediately exposed and released to the mouth of a patient, thereby completely vitiating the purpose of the "degradable material" to controllably release the agent only upon disruption of the water-stable coating and subsequent contact of the degradable material with saliva.

In addition to those noted above, Masterman, et al. also fails to disclose other limitations of independent claim 28. For example, the claimed nanoparticles possess a zeta potential of about 20 millivolts or more. As described in the present specification, the manner in which the functional compound is bonded to the alumina allows the particle to retain a positive surface charge (measured as zeta potential), which in turn allows it to be affixed to various substrates without requiring the use of chemical binders or other attachment structures. The Office Action indicates that such a zeta potential is inherent in Masterman, et al. because the composite particles are made of the "same material (tetracycline adsorbed or chemically bound to alumina)." However, the composite particles of Masterman, et al. are not made of tetracycline bound to alumina, but instead of a degradable material (e.g., poly(DL-lactide)-co-glycolide), mineral, anti-microbial agent, and water-stable coating (e.g., polystyrene). There is simply no indication that such a composite would "necessarily" posses the claimed zeta potential as is required to establish a prima facie case of inherency.

Masterman, et al. also fails to disclose that the nanoparticles are contained within a vehicle that further comprises a pH altering material so that the functional compound is released from the surface of the nanoparticles upon exposure to a change in pH. Nevertheless, the Office Action cited Ma, et al. for the teaching of the release of the

anti-microbial agent of Masterman, et al. upon a change of pH. Ma, et al. describes the adsorption of tetracycline on alumina membranes as pH dependent. This teaching alone, however, would in no way lead one of ordinary skill in the art to the modification suggested in the Office Action. Thus, for at least the reasons indicated, Applicants respectfully submit that independent claim 28 patentably defines over the cited references.

The Office Action also rejected dependent claim 43 (now incorporated into independent claim 28) under *35 U.S.C. § 103(a)* as being obvious over U.S. Patent No. 5,785,977 to Breithbarth in view of U.S. Patent No. 6,548,264 to Tan, et al. Breithbarth is directed to non-metallic microparticles (e.g., silica, charcoal, alumina, or boron) having an electrical surface charge that has been adjusted so that they can serve as carrying agents for pharmaceutical and cosmetic agents. However, Breithbarth fails to disclose various limitations of the present claims. For instance, as correctly acknowledged by the Examiner, Breithbarth fails to disclose the use of a plurality of nanoparticles containing silica coated with alumina. The Office Action nevertheless cites Tan, et al. as teaching this feature.

Tan, et al. describes core-shell nanoparticles in which the core may be a magnetic material (e.g., magnetite), metal or metal salt (e.g., gold), and so forth, and the shell may be silica or alumina. While Tan, et al. may generally described alumina- or silica-coated nanoparticles, however, it does not disclose or suggest the claimed alumina-coated *silica nanoparticles*. In any event, Breithbarth and Tan, et al. fail to disclose or suggestion other limitations of the present claims. For example, the references fail to disclose that the nanoparticles are contained within a vehicle that

further comprises a *pH altering material* so that the functional compound is released from the surface of the nanoparticles upon exposure to a change in pH, as required by the present claims. Moreover, the modification proposed in the Office Action would also contradict the express teachings of Breithbarth. Namely, according to Breithbarth, "it is preferred that the microparticles have a substantial negative charge." (Col. 3, ll. 1-3). If the microparticles of Breithbarth were modified with alumina, it is Applicants' understanding that they would have a positive charge.

Applicants emphasize that none of the cited references recognize the benefits achieved according to the present claims. Namely, the functionalized nanoparticles of the present claims may retain a positive surface charge, which can provide a variety of benefits. For example, the nanoparticles may better adhere to substrates that carry a negative surface charge *via* coulombic attraction. Consequently, a functional compound may be affixed to the substrate without the use of chemical binders or other attachment structures. Further, the nanoparticles may also better adhere to skin, mucosal membranes, etc. due to their high zeta potential. Thus, for at least the reasons set forth above, Applicants respectfully submit that the present claims patentably define over the cited references, taken singularly or in any proper combination.

It is believed that the present application is in complete condition for allowance and favorable action, therefore, is respectfully requested. Examiner Schlientz is invited and encouraged to telephone the undersigned, however, should any issues remain after consideration of this Amendment.

Please charge any additional fees required by this Amendment to Deposit Account No. 04-1403.

Respectfully requested,

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Date: 3/17/08